REMARKS

Status of the Claims

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

In the specification, paragraphs have been amended on page 1.

Claims 13 and 14 are requested to be cancelled. Applicant reserves the right to pursue the subject matter of the canceled claims in subsequent divisional applications. The cancellation of claims does not constitute acquiescence in the propriety of any rejection set forth by the Examiner.

Claim 1 is currently being amended. Exemplary support for the amendment is found in claims 13 and 14.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claims remain under examination in the application, is presented, with an appropriate defined status identifier.

Upon entry of this Amendment, claims 1-12 and 15-42 will remain pending in the application, with claims 21-41 withdrawn from consideration as a result of a Restriction Requirement and claims 1-12 and 15-20 ready to be examined on the merits.

Issues Under Specification

The Examiner objects to the specification because the first line of the specification needs to be updated to claim priority to the provisional application 60/220,782, filed July 25, 2000. Applicant has amended the specification as suggested by the Examiner. Therefore, Applicant respectfully requests reconsideration and withdrawal of the objection.

35 U.S.C. § 112, Second Paragraph

Claims 5, 7 and 8 are rejected by the Examiner as being indefinite. Applicant respectfully requests reconsideration and withdrawal of the rejection.

The Examiner asserts that the term "derivative" is not one which ahs a universally accepted meaning in the art nor is it one which has been adequately defined in the specification. Applicant respectfully disagrees with the Examiner and directs the Examiner's attention to page 10, lines 10-18 of the specification where the specification provides a definition for the term "derivative" and references WO 93/11236 for methods of constructing such compounds. Therefore, a person of ordinary skill in the art would know the metes and bounds of the term "derivative."

Claim Rejections - 35 U.S.C. § 102

A. Rejection of claims 1-7, 9-12, and 16-19 as being anticipated by Schoonjans et al.

Claims 1-7, 9-12 and 16-19 are rejected by the Examiner under 35 U.S.C. § 102 as being anticipated by Schoonjans et al. (WO 99/37791). Applicant respectfully requests reconsideration and withdrawal of the rejection.

The Examiner asserts that the invention of Schoonjans et al. anticipates the present invention. Applicants do not agree. However, to expedite prosecution, Applicants have amended claim 1 to include the subject matter of claims 13 and 14. Claim 13 (now canceled) was directed to a target binding protein of claim 1, wherein either the first polypeptide or the second polypeptide further comprises a N-glycosylation recognition sequence. Claim 14 (now canceled) was directed to the binding protein of claim 13, wherein a carbohydrate chain is linked to the N-glycosylation recognition sequence. Schoonjans et al. fails to teach or suggest the subject matter of canceled claims 13 and 14, the subject matter of which has been added to claim 1. Therefore, claims 1-7, 9-12, and 16-19, as amended, are not anticipated by Schoonjans et al.

B. Rejection of claims 1-2 and 9-10 as being anticipated by Harris et al. (WO 94/09131)

Claims 1-2 and 9-10 are rejected by the Examiner under 35 U.S.C. § 102 as being anticipated by Harris et al. (WO 94/09131). Applicant respectfully requests reconsideration and withdrawal of the rejection.

The Examiner asserts that the invention of Harris et al. anticipates the present invention. Applicants do not agree. However, to expedite prosecution, Applicants have amended claim 1 to include the subject matter of claims 13 and 14. Claim 13 (now canceled) was directed to a target binding protein of claim 1, wherein either the first polypeptide or the second polypeptide further comprises a N-glycosylation recognition sequence. Claim 14 (now canceled) was directed to the binding protein of claim 13, wherein a carbohydrate chain is linked to the N-glycosylation recognition sequence. Harris et al. fails to teach or suggest the subject matter of canceled claims 13 and 14, the subject matter of which has been added to claim 1. Therefore, claims 1-2 and 9-10, as amended, are not anticipated by Harris et al.

Claim Rejections - 35 U.S.C. § 103

A. Rejection of claims 1-20 as being obvious over Schoonjans et al. in view of Leung et al. and Lindhofer et al.

Claims 1-20 are rejected by the Examiner under 35 U.S.C. § 103 as being obvious over Schoonjans et al. (WO 99/37791) as applied to claims 1-7, 9-12, and 16-19 above, and further in view of Leung et al. (U.S. Patent No. 6,254,868) and Lindhofer et al. (U.S. Publication No. 20002/0051780). The Examiner asserts that although Schoonjans et al. does not teach a N-glycosylation site, a toxin linked to the carbohydrate site, the linkers of SEQ ID NOS:1 and 2, or that the molecules bind to CD28 and CD3, these deficiencies are made up for by the teachings of Leung et al. and Lindhofer et al. Applicant respectfully requests reconsideration and withdrawal of the rejection.

A proper rejection for obviousness under §103 requires consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition, or device, or carry out the claimed process and (2)

whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure. [emphasis added] *In re Vaeck*, 947 F.2d 488, 493, 20 USPQ2d 1438 (Fed. Cir. 1991). In the pending case, the examiner has failed to establish a *prima facie* case of obviousness.

Leung et al. is directed to a humanized specific monoclonal antibody or antibody fragment engineered to contain a glycosylation site in the non-Fc constant region. In contrast, the present invention is directed to a target binding protein comprising a first polypeptide comprising a first scFv and a first immunoglobulin-like domain and a second polypeptide comprising a second scFv and a second immunoglobulin-like domain wherein said first and second scFv each form two target binding sites independently, or wherein said first scFv associates with said second scFv to form two target binding sites; wherein said first immunoglobulin-like domain associates with said second immunoglobulin-like domain to form a third target binding site; wherein either the first polypeptide or the second polypeptide further comprises a N-glycosylation recognition sequence; and wherein a carbohydrate chain is linked to the N-glycosylation recognition sequence. There is no teaching or suggestion in Leung et al. to engineer a compound other than a monoclonal antibody to contain a glycosylation site in the non-Fc constant region.

Furthermore, a person of ordinary skill in the art would know that the human monoclonal antibody of Leung et al. is an entirely different compound with entirely different properties than the target binding protein of the present invention. For example, a person of ordinary skill in the art would expect that the monoclonal antibody of Leung et al. would have different secondary and/or tertiary structure than the target binding protein of the present invention. As a result, a person of ordinary skill in the art would know that an engineering process that was successful for a monoclonal antibody may be unsuccessful for the target binding protein of the present invention.

At best, the examiner is using an improper "obvious to try" standard, arguing that it would have been obvious to a person of ordinary skill in the art to modify the teachings of

Schoonjans et al. with the teachings of Leung et al. and Lindhofer et al. to obtain the target binding protein of the present invention. However, "'obvious to try' has long been held to not constitute obviousness." *In re Deuel*, 51 F.3d 1552, 1559, 34 USPQ2d 1210 (Fed. Cir. 1995).

Lindhoffer et al. is directed to intact bispecific or trispecific antibodies which simultaneously bind to the T cell receptor complex of a T cell, to tumour-associated antigens on a tumor cell, and to Fc receptor-positive cells. The teachings of Lindhoffer et al. do not cure the deficiencies of Schoonjans et al. and Leung et al. Therefore, claims 1-20 are not obvious over Schoonjans et al. in view of Leung et al. and Lindhofer et al.

B. Rejection of claims 1-2, 9-10 and 11-18 as being obvious over Harris et al. in view of Chaudhary et al. and Leung et al.

Claims 1-2, 9-10, and 11-18 are rejected by the Examiner under 35 U.S.C. § 103 as being obvious over Harris et al. (WO 94/09131) as applied to claims 1-2 and 9-10 above, in view of Chaudhary et al. (PNAS 87:1066-70, 1990) and Leung et al. (U.S. Patent No. 6,254,868). The Examiner asserts that although Harris et al. does not teach a conjugate at the C-terminal of the polypeptide, a glycosylation site for conjugations to toxins, or binding to toxin and tumor antigens, these deficiencies are made up for in the teachings of Chaudhary et al. and Leung et al. Applicant respectfully requests reconsideration and withdrawal of the rejection.

As discussed above, Leung et al. is directed to a humanized specific monoclonal antibody or antibody fragment engineered to contain a glycosylation site in the non-Fc constant region. In contrast, the present invention is directed to a target binding protein comprising a first polypeptide comprising a first scFv and a first immunoglobulin-like domain and a second polypeptide comprising a second scFv and a second immunoglobulin-like domain wherein said first and second scFv each form two target binding sites independently, or wherein said first scFv associates with said second scFv to form two target binding sites; wherein said first immunoglobulin-like domain associates with said second immunoglobulin-like domain to form a third target binding site; wherein either the first

polypeptide or the second polypeptide further comprises a N-glycosylation recognition sequence; and wherein a carbohydrate chain is linked to the N-glycosylation recognition sequence. There is no teaching or suggestion in Leung et al. to engineer a compound other than a monoclonal antibody to contain a glycosylation site in the non-Fc constant region.

Furthermore, a person of ordinary skill in the art would know that the human monoclonal antibody of Leung et al. is an entirely different compound with entirely different properties than the target binding protein of the present invention. For example, a person of ordinary skill in the art would expect that the monoclonal antibody of Leung et al. would have different secondary and/or tertiary structure than the target binding protein of the present invention. As a result, a person of ordinary skill in the art would know that an engineering process that was successful for a monoclonal antibody may be unsuccessful for the target binding protein of the present invention.

At best, the examiner is using an improper "obvious to try" standard, arguing that it would have been obvious to a person of ordinary skill in the art to modify the teachings of Schoonjans et al. with the teachings of Leung et al. and Lindhofer et al. to obtain the target binding protein of the present invention. However, "'obvious to try' has long been held to not constitute obviousness." *In re Deuel*, 51 F.3d 1552, 1559, 34 USPQ2d 1210 (Fed. Cir. 1995).

Chaudhary et al. is directed to a method to rapidly clone the functional variable region sequences of many different antibodies for hybridoma RNA. The teachings of Chaudhary et al. doe not cure the deficiencies discussed above of Harris et al. and Leung et al. Therefore, claims 1-2, 9-10 and 11-18 are not obvious over Harris et al. in view of Chaudhary et al. and Leung et al.

CONCLUSION

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant(s) hereby petition(s) for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date February 27, 2004 By _____

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